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Original

Influence of an immuno-enhanced formula in postsurgical ambulatory patients with head and neck cancer

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Abstract

Background: Patients with head and neck cancer undergoing surgery have a high incidence of ambulatory postoperative complications.

Objective: The aim of our study was to investigate the influence of an oral immunoenhanced supplement (arginine and glutamine) on nutritional and biochemical parameters in postsurgical ambulatory patients with head and neck tumor.

Design: A population of 39 ambulatory postsurgical patients with oral and laryngeal cancer was enrolled. At Hospital discharge postsurgical head and neck cancer patients were asked to consume two units per day of a specially designed enhanced supplement for a twelve week period.

Results: The mean age was 60.2+/-13.1 years (9 female/30 males). Duration of supplementation was 90.8+20 days. A significant increase of albumin (3.1±0.6 g/dl vs 4.12±0.7 g/dl; p<0.05), prealbumin (21.4±6.3 mg/dl vs 22.4±5.9 mg/dl; p<0.05) and transferrin (198.8±45.2 mg/dl vs 253.8±60.7 mg/dl; p<0.05) levels were observed. No differences were detected in weight and other anthropometric parameters. Ten patients (41.3%) received radiotherapy along the enhanced supplementation period and only 5 (20% of patients with radiotherapy) developed a clinical oral mucositis.

Conclusions: At dose used, arginine and glutamine enhanced formula improved seric protein levels in ambulatory postoperative head and neck cancer patients with a low rate of oral mucositis in the subgroup with radiotherapy.

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Key words: Ambulatory. Arginine. Glutamin. Head and neck cancer. Immunonutrition.

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Introduction

Patients with head and neck cancer undergoing surgery have a high incidence of malnutrition and it is known that immune system is frequently affected in these patients. Although immune dysfunction could be multifactorial, this immune system may be modulated by specific nutritional substrates, such as omega-3 fatty acids. Administration of n-3 fatty acid or high purity EPA capsules has been associated with weight stabilization in patients with pancreatic cancer. Good tolerance and an improvement on serum proteins have been demonstrated in patients with head and neck cancer. Arginine is another immunonutrient that could play an important role in this type of patients. It has demonstrated in head and neck cancer patients with enteral arginine enhanced after surgery an improvement in weight and complications rate. For patients with head-and-neck cancer receiving radiotherapy, glutamine has been demonstrated as an effective preventive measure to decrease the severity of mucositis.

The aim of our study was to investigate the influence of an oral immunoenhanced supplement (arginine and glutamine) in nutritional and biochemical parameters in postsurgical ambulatory patients with head and neck tumor.

Material and methods

Patients

A population of 39 ambulatory postsurgical patients with oral and laryngeal cancer was enrolled. Exclusion criteria included: severy impaired hepatic function (total bilirubin concentration >3.5 mg/dl) and renal function (serum creatinine concentration >2.5 mg/dl), ongoing infections, major gastrointestinal disease, autoimmune disorders, steroids treatment, and medication could modulate metabolism or weight. The study was prospective and carried out from May 2007 to May 2009. Baseline studies on all patients at the moment of Hospital discharge after surgery consisted of complete history taking and physical examination. General assessment of nutritional status included measurements of height, body weight, body mass index (kg/m²), circumferences and tricipital skinfold of the midarm with an additional bio impedance.

Nutrition

At Hospital discharge postsurgical head and neck cancer patients were asked to consume two units per day of a specially designed immunoenhanced supplement (enriched with arginine and glutamine: Impact oral (r) plus Resource glutamina (r)) for a twelve week period. Table I shows the composition of the supplement. Three day diet diaries completed at baseline (week 0), and weeks 12 were used to assess the patient’s dietary intakes. One weekend day and two weekdays were studied to account for potential day of the week effects on dietary intake. A dietitian instructed patients on how to record food and beverage intake. Mean total energy and macronutrient intakes were calculated using country specific computerized dietary analysis packages. Total dietary intake was calculated by adding oral supplement consumption to spontaneous food intake, asking to record the number of bricks of supplements or parts therefore.

Patient monitoring

At the initial assessment body weight was measured to an accuracy of 0.5 Kg and body mass index computed as body weight/(height²). Bipolar body electrical bioimpedance was used to determine body composition. An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (Biodynamics Model 310e, Seattle, WA, USA) and applied to the skin using adhesive electrodes placed on right-side limbs. Resistance and reactance were used to calculate total body water, fat and fat-free mass. Regional changes in body mass were estimated by measuring the circumferences and tricipital skinfold of the midarm. Radiotherapy treatment was recorded and the presence of mucositis too. Ambulatory postoperative complications were recorded as none, general infections (respiratory tract infection and/or urinary tract infection) and local complications such as fistula and/or wound infection, assessed all complications with standard methods by the same investigator. Gastrointestinal problems related to enteral feeding were also recorded (diarrhea or vomiting).

Assays

Fasting blood samples were drawn for measurement of, albumin (3.5-4.5 gr/dl), prealbumin (18-28 mg/dl), transferrin (250-350 mg/dl), and lymphocytes (1.2-3.5.10³/uL) with an auto analyzer (Hitachi, ATM, Mannheim, Ger). CRP (c-reactive protein) was measured by immunoturbimetry (Roche Diagnostics GmbH, Table 1

<table>
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<tr>
<th>Composition of supplement</th>
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<tr>
<td>Total energy(Kcal)</td>
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<tr>
<td>Protein (g)</td>
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<tr>
<td>Free L-arginine</td>
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<tr>
<td>Casein</td>
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<tr>
<td>Total lipid (g)</td>
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<td>W6</td>
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<td>W3</td>
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<td>MCT</td>
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<tr>
<td>Carbohydrate (g)</td>
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<tr>
<td>Dietary fiber (g)</td>
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<td>Glutamine (g)</td>
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Dietary fiber: guar gum from Impact oral (r). Glutamine was added as a powder formula to the original immunoenhanced formula from Resource glutamine (r).
Mannheim, Germany), analytical sensitivity 0.5 mg/dl. Samples were assayed in duplicate in one day by the same investigator to avoid inter-investigator variability.

**Statistical analysis**

The results were expressed as mean standard deviation. The distribution of variables was analyzed with Kolmogorov-Smirnov test. Quantitative variables with normal distribution were analyzed with two tailed paired or unpaired Student’s t-test, as needed and analysis of variance (ANOVA). Non-parametric variables were analyzed with the Friedman and Wilcoxon tests. A p-value under 0.05 was considered statistically significant.

**Results**

Thirty nine patients were enrolled in the study. The mean age was 60.2±13.1 years (9 female/30 males). Epidemiological data of population are shown in table II. Duration of supplementation was 90.8±20 days.

Total calorie and protein consumption, based on both formula and dietary intake with 3 days food records, was (calories 2252±865 kcal/day) and (proteins: 100.1±26.4 g/day). As shown in table III, a significant increase of albumin, prealbumin and transferrin levels were observed. No differences were detected in weight and other anthropometric parameters (table IV).

Gastrointestinal tolerance (diarrhea and vomiting) was good, without cases during the protocol follow up. There were no dropouts due to intolerance. Ten patients (41.3%) received radiotherapy along the enhanced supplementation period and only 5 (20% of patients with radiotherapy) developed a clinical oral mucositis.

**Discussion**

Malnutrition and immunosupression were two factors of head and neck cancer patients. There is a body of evidence suggesting that enteral feeding; supplemented with immunomodulatory agents including arginine and glutamine reduce postoperatively complications. The main result of our open study is a significant increase on serum protein levels after this supplementation with a low rate of oral mucositis episodes.

Our group has demonstrated in head and neck cancer patients with enteral arginine enhanced after surgery an improvement in weight and complications rate, during Hospital stance. However, all these previous studies have been performed with income patients, with a short period of enteral nutrition. In our study, we analyze ambulatory patients during three months of oral supplementation, with a significant increase in seric protein levels and no changes in anthropometric parameters. Taking account, the low rate of adverse effects and the improvement in this biochemical parameters, this strategy of nutritional oral supplementation could be a way to treat this ambulatory patients.

Polymeric formulas are suitable for head and neck cancer patients, considering that the gastrointestinal tract distal to the oropharynx is usually normal and the digestion and absorption functions are intact. Various studies demonstrate that early use of enteral feedings during head and neck cancer treatment reduces weight loss, malnutrition, dehydration and the associated need for hospitalization or treatment interruption. However, immunoenhanced formulas could be used, too due to specific problems of these type of patients such as mucositis and coadjuvants treatments.
Oral mucositis appeared in 80% of patients with head and neck cancer receiving radiotherapy. Our patients had oral mucositis in a low rate (20% of the patients with radiotherapy). Although our design is not a randomized clinical trial, the incidence of oral mucositis is lower than previously reported in the literature. Glutamine, a non-essential aminoacid widely distributed throughout the body, can behave as an essential amino acid in certain clinical settings. A number of studies have also examined the use of enteral glutamine or the treatment a prevention of mucositis. Although our daily dose of glutamine was lower (10 g per day or 0.15 g per kg and day), perhaps the glutamin administration in a viscous vehicle (such as Impact oral) that will allow it to “stick” the mucosa could explain the low rate of mucositis in patients with radiotherapy.

In conclusion, at dose used, arginine and glutamine enhanced formula improved seric protein levels in ambulatory postoperative head and neck cancer patients with a low rate of oral mucositis in the subgroup with radiotherapy. Further randomized studies will be needed to confirm these preliminary results and to avoid potential bias.

References